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Award Number: DAMD17-03-1-0138

TITLE: Cognitive Performance, Quality of Life, and Psychosocial
Adjustment Among Men Receiving Androgen Deprivation
Therapy for Treatment of Prostate Cancer

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REPORT DATE: April 2005

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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20050826 111

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE April 2005	3. REPORT TYPE AND DATES COVERED Annual Summary (1 Apr 03 - 31 Mar 05)	
4. TITLE AND SUBTITLE Cognitive Performance, Quality of Life, and Psychosocial Adjustment Among Men Receiving Androgen Deprivation Therapy for Treatment of Prostate Cancer			5. FUNDING NUMBERS DAMD17-03-1-0138	
6. AUTHOR(S) Pamela J. Shapiro, Ph.D. James C. Coyne, Ph.D. David J. Vaughn, M.D. Rosette Plotkin Biester, Ph.D.				
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9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 Words) The goal of the original research study proposed in this postdoctoral training grant were to a) determine the prevalence and degree of cognitive impairment in men receiving androgen deprivation therapy (ADT) for treatment of PC relative to age-matched norms; and b) determine whether cognitive impairment in men receiving ADT is more severe than that of PC patients who are not receiving ADT. In addition, this pilot study examined relationships between subjective reports of cognitive impairment and objective measurement of cognitive performance, and assessed relationships among fatigue, psychological distress, quality of life (QOL) and cognitive function. Objective cognitive performance, subjective cognitive complaints, fatigue, and distress did not differ between men receiving ADT and controls. Men in both treatment groups experienced clinically meaningful deficits in cognitive function relative to norms. Younger men (<65 years) performed more poorly on measures of executive function ($ps < .02$), however sample size precludes attributing this difference to age-associated differential effects of treatment. Higher levels of psychological distress were associated with lower overall QOL ($p < .001$), greater fatigue ($ps < .02$), and poorer subjective cognitive function ($ps < .008$). Treatment of psychological distress may attenuate cognitive symptoms, decrease fatigue, and improve overall QOL for men with PC.				
14. SUBJECT TERMS Prostate Cancer, Cognitive Function, Quality of Life, Testosterone			15. NUMBER OF PAGES 7	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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Introduction

This project is an individual postdoctoral training grant in prostate cancer. The project involves focused mentorship and training in all aspects of prostate cancer, including psychosocial and quality of life issues. The training plan includes opportunities for secondary data analyses as well as an original research project focusing on neurocognitive sequelae of androgen deprivation therapy (ADT). Suppression of testosterone by androgen deprivation therapy is the preferred treatment for advanced prostate cancer (PC) and in recent years has been increasingly prescribed for treatment of early stage PC. Although many of the side effects of ADT have been well-documented, potential cognitive impairment associated with ADT has been neglected in the literature. In our preexisting pilot data, 35% of men receiving ADT reported moderate to severe difficulties with attention, concentration, and memory, suggesting that in addition to normal age-related declines in cognitive function, men receiving ADT may experience hormone-related cognitive impairments that remain undetected and untreated. The present study describes the nature and prevalence of objectively assessed cognitive difficulties in PC patients treated with ADT, examines the relationship between subjective reports of cognitive impairment and objective measurement of cognitive performance, and assesses relationships among fatigue, psychological distress, quality of life (QoL), and cognitive function.

Body

This project is received notice of award on October 31st, 2002 and notification of final approval on March 1st 2003 stating that the grant contract was signed and scheduled to begin on April 1st, 2003. Previously reported training and research activities in accord with the original proposal and Statement of Work included completion of preparatory tasks (Tasks 1, 3, and 4) and initiation/continuation of training (Task 2), secondary data analyses and manuscript preparation (Task 6), subject recruitment and data collection for primary research project (Task 5), interim analyses and presentation of preliminary results at professional meetings (Task 7).

Research Project

Since the last report, data collection for the original research project continued. In an effort to increase accrual and include a greater diversity of men with PC, recruitment was extended into the larger Penn and Philadelphia communities by distribution of flyers at support groups, local conferences, the Hospital of the University of Pennsylvania (HUP), and Penn affiliated Presbyterian Hospital. Efforts to recruit from HUP urology clinics were unsuccessful, as the clinic staff found direct recruitment burdensome. The majority of participants were drawn from Dr. David Vaughn's Genitourinary Cancer Program where our research staff was allowed to approach patients directly. Despite continued efforts, the study team was unable to attract sufficient numbers of eligible men, particularly non-ADT controls, who do not regularly attend clinic.

To date we have accrued 37 participants, including 26 men receiving ADT and 11 non-ADT controls. Two additional men are scheduled for assessment. Participants are predominantly Caucasian (86%), 11% are African American, and 3% are Asian. Participants ranged in age from 46-83 years ($M = 70$ years), 84% had completed college, graduate school, or professional studies, and 68% reported incomes \geq \$50,000. The majority of men were married or living with a partner (57%), 24% were employed full time and 36% were retired. At point of assessment the mean time since diagnosis was 4 years.

Some aspects of data reduction and analyses continue (Task 8: months 20-24 and post funding), specifically downloading, coding, and transformation of electronic data from the Penn Conditional Exclusion Test (PCET) and the Psychomotor Vigilance Task, and medical chart review for the most recent participants. Results of the data analyses completed to date demonstrate that objective cognitive performance, subjective cognitive complaints, fatigue, and psychological distress did not differ between men receiving ADT and those who had received only local treatment. Men in both treatment groups experienced clinically meaningful deficits (> 1 SD) in cognitive function, particularly in visuospatial memory, verbal memory, and verbal fluency. Younger men (< 65 years) performed more poorly on two measures associated with executive function ($ps < .02$), however sample size precludes attributing these differences to age-associated differential effects of treatment. Inspection of cell means reveals that the younger men who had only local treatment (surgery or surgery-plus-radiation) performed more poorly on these tasks. Men receiving ADT reported lower physical well-being $p = .05$, but other QOL domains did not differ as a function of treatment. Higher levels of psychological distress were associated with lower QOL across domains ($p < .001$), as well as greater fatigue ($ps < .02$), and poorer subjective cognitive function ($ps < .008$).

Overall 41% of the men in this sample experienced significant deficits in one or more cognitive domains and should be reevaluated for further decline in two years. Cognitive remediation should be offered to men with clinically relevant mild cognitive impairment (MCI). Cognitive complaints among PC patients may indicate the presence of psychological distress, and patients reporting cognitive difficulties should be evaluated for psychiatric comorbidity and treated accordingly, as treatment of psychological distress may attenuate certain cognitive symptoms, decrease fatigue, and improve overall QOL.

Education and Career Development

In addition to the training and career development activities reported in the 2004 annual report, Dr. Shapiro has completed the Biomedical Postdoctoral Programs Research Success Skills Series seminars in scientific writing, public speaking, lab management, and grant writing. She served on the Biomedical Postdoctoral Council and as a postdoctoral representative to the committee for Standards for Scientific Conduct among Postdoctoral Researchers and Staff. She has continued to attend the Grand Rounds and speaker series sponsored by the Abramson Cancer Center, the Center for Clinical Epidemiology and Biostatistics, Neuropsychiatry, and the Department of Psychiatry of the University of Pennsylvania. In addition, she has participated in and presented at the regular meetings of the Behavioral Oncology Group of the Division of Cancer Control and Outcomes and has completed seminars in statistics, including strategies for design and data analyses in clinical trials and analysis of qualitative data (N-Vivo).

Key Research Accomplishments

- All aspects of the project were carried out according to the plan described in the original proposal, although we were unable to meet the projected subject accrual.
- Interim results were reported at professional conferences
- Final analyses are under way. Because of the small N, strategies for publication have been altered, and these results will be incorporated into a paper reviewing QOL in PC and including a review of neurocognitive studies of men receiving ADT.

Reportable Outcomes

Manuscript in Preparation

Shapiro, P. J., Coyne, J.C., & Vaughn, D. J. (2005). *Crossing Domains: Quality of life in men with prostate cancer*. Manuscript in preparation.

Grants in Preparation

I am currently assembling a mentor team for a career development/transition award focusing on neurocognitive sequelae of cancer and cancer-related treatment across disease sites.

Peer Reviewed Publications and Presentations

- Shapiro, P. J., Jacobs, L. A., Palmer, S. C., Coyne, J. C., Meadows, A. T., & Vaughn, D. J., (In Press). *Neurocognitive function in long-term survivors of testicular cancer*. [Abstract] Proceedings of the American Society of Clinical Oncology 2005 Annual Meeting.
- Shapiro, P. J., Coyne, J. C., Kruus, L. K., Palmer, S. C., Malkowicz, S. B., Vaughn, D. J. (2004). Interest in services among prostate cancer patients receiving androgen deprivation therapy. *Psycho-Oncology*, 13, 512-525.
- Coyne, J.C., Palmer, S.C., Shapiro, P. J. (2004). Prescribing antidepressants to advanced cancer patients with mild depressive symptoms is not justified: Response to Fisch et al. [Letter to the editor]. *Journal of Clinical Oncology*, 22, 205-206.
- Shapiro P. J., Butterfield, L.C., Coyne, J.C., Beister, R.C., Matthews, G., & Vaughn, D.J. (July, 2004). *Cognitive Function among Men Receiving Androgen Deprivation Therapy*. Poster presented at the Annual Convention of the American Psychological Association, Hawaii.
- Shapiro, P. J., Diefenbach, M. A., Eton, D. T., & Lepore, S. (2004, March) Factors affecting quality of life among prostate cancer patients: Current knowledge and new directions. [Symposium Abstract] *Annals of Behavioral Medicine*, 27, S169.
- Shapiro, P. J., Coyne, J.C., Butterfield, L. C., Plotkin, R. C., Malkowicz, S. B., & Vaughn, D. J. (2004, March). Cognitive performance, psychological distress, and quality of life among men receiving androgen deprivation therapy for treatment of prostate cancer. [Abstract] *Annals of Behavioral Medicine*, 27, S170.
- Butterfield, L.C., & Shapiro, P. J. (2004, February). *Cognitive complaints, cognitive performance, and psychological distress among men with genitourinary cancers*. Poster presented at the annual meeting of the International Neuropsychological Society, Baltimore.
- Shapiro, P. J. (2003, March) *Cognitive performance, quality of life, and psychosocial adjustment among men receiving androgen deprivation therapy for treatment of prostate cancer: Design and methods*. Paper presented at the New Investigators Workshop of the annual meeting of American Society of Preventive Oncology, Philadelphia.

Invited Talks

- *Neuropsychological sequelae of cancer and cancer-related treatment*. Talk presented at The University of Pennsylvania Cancer Control and Outcomes Meeting. June 8, 2004

- *Examining Cognitive Performance among Men Receiving ADT for treatment of Prostate Cancer: Why Prostate Cancer? Why Now?* Talk presented at the Psychosocial-Oncology Seminar at the University Of Pennsylvania School Of Nursing. May 15, 2003.
- *Studying Memory, Attention and Reasoning among Men Treated for Prostate Cancer: Subjective Complaints vs. Objective Measurement.* Talk presented at The University of Pennsylvania Prostate Cancer Support Group. June 17, 2003.

Employment Opportunities

- Applications for research/teaching positions are under review as my fellowship comes to an end in November 2005.

Conclusions

Men receiving ADT for treatment of PC experience significant decrements in physical well-being. Although, men with PC experienced deficits in cognitive function, these cannot be attributed to a specific treatment. Younger men appear to have greater difficulty in tasks associated with executive processing, however the reason for this is unclear. Psychological distress is associated with greater fatigue, more subjective cognitive difficulties, and overall poorer QOL. Additional analyses are underway to better understand the direction of these relationships.

References None

Appendices None